REMARKS/ARGUMENTS

The Official Action dated December 18, 2002 has been carefully considered. It is believed that the following comments represent a complete response to the Examiner's rejections and place the present application in condition for allowance. Reconsideration is respectfully requested.

35 U.S.C. § 121

A restriction to one of three inventions was requested by the Examiner pursuant to 35 U.S.C. § 121. The election made on 10/18/02 to prosecute the invention of Group I, Claims 1-19, is affirmed in this present response. As such, Claims 27 and 28 are withdrawn without prejudice, especially without prejudice to any right to pursue such claims in a subsequent divisional or continued application. Similarly, claims 20-26 were previously cancelled without prejudice to any right to pursue such claims in a subsequent divisional or continued application.

35 U.S.C. § 112

The Examiner rejected claims 1-19 as being indefinite pursuant to 35 U.S.C. § 112. In addition, the Examiner opposed the combination of Claim 1 and 7 as vague and indefinite because Claim 7 (dependent) is broader than Claim 1 (independent).

Applicant does not necessarily agree that claim 7 was broader than claim 1, however, the Applicant has amended Claims 1 and 7 for consistency. Claim 1 was amended to indicate that charged dextran is administered to the respiratory tract mucus of an animal. The Applicant respectfully submits that this amendment overcomes the Examiner's rejection. Claim 7 has also been amended accordingly.

35 U.S.C. § 102

The Examiner rejected Claims 1, 4-5 and 7-8 as being anticipated by Beller *et al.* (Am. J. Obstet Gynecol 1986). The Applicant submits that Beller *et al.* discloses the use of dextran sulfate for a substance that is chemically different from respiratory tract mucus. In particular, respiratory tract mucus is different from the "gastrointestinal mucus" described in Beller *et al.*., both in its physical properties and in its biological role. The Examiner appears to have

recognized this difference but indicated that the claims are not limited to respiratory tract mucus. The Applicant respectfully notes that Claim 1 is limited to respiratory tract mucus and has amended claim 1 to clarify this. As Claims 4-5 and 7-8 are dependant on Claim 1 they would also have this limitation. As such it is respectfully submitted that Beller *et al.* does not anticipate Claims 1, 4-5 and 7-8.

35 U.S.C. § 103

The Examiner objected to Claims 1-2, 4-5, 7-17 as unpatentable under 35 U.S.C. 103(a) because of Speert *et al.* (US Patent No. 5,514,665). In addition, the Examiner rejected Claims 3, 6, 18-19 as obvious over Speert *et al.* and Kennedy (WO 91/16216). The Applicant respectfully submits that neither Speert *et al.* nor Kennedy teaches a method of altering the viscosity or clearability of respiratory tract mucus. Speert *et al.* discloses the use of dextran sulfate as an anti-adhesive agent to inhibit attachment of bacteria to epithelial cells in cystic fibrosis patients, and Kennedy teaches the molecular weights of dextran sulfate. Neither reference teaches in combination or alone, the method of using dextran sulfate in patients that are not afflicted with respiratory tract bacterial infection but still would benefit from improved mucus clearability. Such conditions include, but are not necessarily limited to, asthma and chronic obstructive pulmonary disease (COPD).

In *Bristol-Myers Squibb Co.* v. *Ben Venue Labs* (2001), 246 F.3d 1368, the Court held that claims directed to a known composition and a known method of use directed to the same purpose as the prior art were anticipated. The Court stated at p. 1376 that "[n]ewly discovered results of known processes directed to the same purpose are not patentable because such results are inherent" [Emphasis added]. A similar holding was made in *In re May* (1978), 574 F.2d 1082. However, it is well established and the Courts recognized that a claim directed to a new use of a known compound is patentable.

In the present invention, dextran sulfate is administered for a purpose and use different from that in Speert *et al.* and Kennedy. It is administered to respiratory tract mucus for a different purpose that is not inherent from Speert *et al.* and Kennedy. The properties of dextran sulfate with respect to respiratory tract mucus are novel and independent of its properties as described in relation to bacterial infections in Speert *et al* and Kennedy.

The Examiner states that Speert *et al* discloses the same method of administering the same composition and implies that the claims of the present application are inherent in light of the prior art cited. It should be noted that Applicant has amended the claims without prejudice to include the limitation, "in an animal that does not have a respiratory tract bacterial infection and not for the purposes of treating a respiratory tract bacterial infection".

First, Speert *et al*, as stated in Applicant's reply to the previous office action, is directed to its use in interfering with the binding of bacteria to buccal or epithelial cells. In fact the examples in Speert *et al* are with fresh buccal epithelial cells. There are no examples of application of the dextran sulfate to the respiratory tract or to respiratory tract mucus (*in vivo or in vitro*). As such, this indicates that the dextran sulfate in Speert *et al.* is working on sites of bacterial adhesion (buccal or epithelial cells) and not on respiratory tract mucus.

The applications disclosed in Kennedy are directed to inhibiting elastase activity. Kennedy demonstrates that he is directing the use of dextran sulfate on HLE and its substrate by describing this specific function *In vitro* in the examples at page 8, line 22 – page 9, line 25, where no respiratory tract mucus is present. Thus, Kennedy teaches the effect of dextran sulfate on HLE and HLE substrate interaction and not on respiratory tract mucus.

With regard to molecular weight and the Examiner's rejection of claims 3, 6, 18 – 19, in Speert *et al.*, everywhere the use of dextran sulfate is mentioned, the workable molecular weight is stated to be between 8,000 – 1,000,000 (Col. 5, line 34; col. 6, line 9 and 46). At col. 7, line 16, the description states that it is known that dextran sulphate of average molecular weight of 8,000 is absorbed by the body and circulated systemically and delivered to sites of *P. aeruginosa* adhesion. Although, the description states that the dextran sulfate can be administered by aerosol, no examples are provided and no examples of administration to respiratory tract mucus are provided as all examples and the description emphasize application to the cellular sites of bacterial adhesion.

The applications disclosed in Kennedy are directed to inhibiting elastase activity. The examples noted by the Examiner at page 8, line 22 – page 9, line 25,are *in vitro* examples applying the dextran sulfate to HLE and an HLE substrate that does not contain respiratory tract mucus.

It is submitted that there is no indication that a person skilled in the art upon reading Speert *et al.* and Kennedy would use dextran sulfate to affect respiratory tract mucus, alter viscosity of respiratory tract mucus or improve respiratory tract mucus clearance.

There is a need and there are many applications for the use of dextran sulfate on respiratory tract mucus *per se* independent of any role in bacterial infection. Although cystic fibrosis is commonly associated with an opportunistic bacterial airway infection, the major bacterial pathogens in cystic fibrosis patients including *Staphylococcus aureus, Streptococcus pneumoniae, Haemophilus influenzae, Pseudomonas aeruginosa* and *Burkholderia cepacia* (Shale *et al.*, Respiratory Medicine 2003), this is not always the case. In fact there are many respiratory diseases that are often not accompanied by bacterial infections and are not necessarily associated with bacterial infections. For example, in asthma, bacterial infections of the lower airways are uncommon, even in an exacerbation of the condition. Upper airway infections are a common trigger of asthma, but these infections are generally viral in origin. In addition, in chronic obstructive pulmonary disease (COPD), only a minority of patients are chronically colonized by bacteria between exacerbations. Yet in these conditions (e.g. asthma, COPD, and chronic bronchitis), retention of mucous secretions in the airways is a prominent feature (e.g. due to mucous cell hyperplasia and/or ciliary dysfunction due to smoking and/or air pollution exposure) and contributes to the morbidity and mortality of the disease. Neither the prior art of Speert *et al.* and Kennedy would lead a person of skill in the art to the use of dextran sulfate in the treatment of a condition not associated with bacterial infection.

As such it is respectfully submitted that Speert *et al.* and Kennedy, neither alone nor in combination render the present claims as amended obvious.

Claim 1 has been amended without prejudice to pursing any restricted subject matter in a subsequent continuation or continuation-in-part application, or the availability of the doctrine of equivalents, to indicate that the use of dextran sulfate is not in animals having a bacterial infection or for purposes of treating a bacterial infection.

It is submitted that support for this amendment can be found in the application as originally filed.

It is well established that support for claims in the description can be express, implicit or inherent. As such the exact wording in the claim does not need to be found in the description [MPEP 2100-169; *In re Wright*, 866 F.2d 422(1989); *In re Smith*, 481 F.2d 910(1973)]. Further, a patent specification should describe the claimed invention in sufficient detail that one skilled in the art can reasonably conclude that the inventor had possession of the claimed invention [*Vas-Cath, Inc. v. Mahurkar,*, 935 F. 2d 1555].

It is submitted that the description supports that claims as amended and shows that the Applicant was in possession of the claimed application. The Applicant respectfully notes that the Examples in the present application involve studies in healthy dogs, which were free of bacterial infections, and show the value of dextran sulfate administration in improving the rheological properties of airway mucus to make it more easily clearable by ciliary and airflow mechanisms in non-bacterial infection environments. A person skilled in the art would understand that "healthy dogs" would be free of bacterial infections. These Examples support the use of dextran sulfate as a mucoactive agent to improve airway clearance, independent of the role of bacterial infection.

Further, the description of the application describes the use of dextran sulfate to disrupt the ionic and hydrogen bonds of respiratory tract mucus and conditions such as bronchial asthma and chronic bronchitis (see page 11, lines 22-23) that a person skilled in the art would appreciate not to be necessarily associated with bacterial infections. As such, it is submitted that a person skilled in the art would understand that the application describes the use of dextran sulfate to "decrease viscoelasticity of respiratory tract mucus in an animal that does not have a bacterial infection and not for the purposes of treating a bacterial infection".

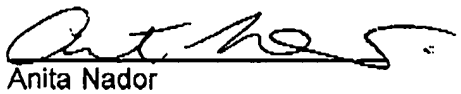
Notes/Suggestions

The Examiner noted that "bronchitis" was spelled incorrectly in Claim 10, line 2 and that the term "form" was spelled incorrectly in Claim 15, line 2. The Applicant has amended the claims accordingly.

In view of the foregoing, it is submitted that the application is in order for allowance and an early indication to that effect would be greatly appreciated. Should the Examiner like to discuss the matter, she is kindly requested to contact Anita Nador at 416-957-1684 at her convenience.

Respectfully submitted,

MALCOLM KING



Anita Nador
Registration No. 47,366

Bereskin & Parr
(Agents for the Applicant)

Box 401, 40 King Street West
Toronto, Ontario, Canada
M5H 3Y2

(416) 364-7311